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Unicentric Castleman Disease With Systemic Symptoms: A Rare Case From Family Practice

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Abstract

Palpable lymphadenopathy is very common in children. The vast majority of cases are due to benign conditions and self-limiting diseases. Careful clinical evaluation, with thorough history taking and make a comprehensive physical examination, is essential to avoid unnecessary invasive procedures and not to misdiagnose possible serious underlying conditions. We report the case of a 9-year-old child with a lump in the right axilla that was first noticed with a swelling two months ago. The lump was not painful but its size has been gradually increasing. The symptom was associated with night sweats. However, there was no history of cough, fever, or weight loss. The child had no history of animal contact or insect bites. No recent travel or history of contact with any sick person was reported. His vaccination schedule was up-to-date. Upon examination, the patient had a smooth non-tender swelling in the right axilla. It measured around 4 x 4 cm. The overlying skin was normal with no erythema or ulceration. The swelling was mobile and was not adherent to the overlying skin. Laboratory investigation showed mild anemia, thrombocytosis, and elevated C-reactive protein level. An ultrasound examination demonstrated a well-circumscribed enlarged lymph node, measuring 3.4 cm in short axis, with an increased blood flow on color doppler. Biopsy findings showed proliferation of the follicular lymphoid tissues that were centered around penetrative vessels giving the appearance of “onion skin” in keeping with Castleman disease. Complete surgical resection of the lymph node was performed and resulted in the resolution of the systemic symptoms. Castleman disease is a rare lymphoproliferative disorder with shared histopathological features. Unicentric Castleman disease usually presents with isolated asymptomatic lymphadenopathy. However, the present case demonstrated that patients with unicentric Castleman disease may exhibit systemic constitutional symptoms similar to that of the multicentric subtype.

Categories: Family/General Practice, Pediatrics
Keywords: lymphadenopathy, castleman disease, night sweats, lymphoproliferative disoder, case report

Introduction

Palpable lymphadenopathy is a common finding in children. It is reported that up to 90% of children may have enlarged lymph nodes due to various etiologies [1]. The differential diagnosis of peripheral lymphadenopathy is very broad. However, the majority of cases are due to benign conditions [1]. Hence, it is crucial to have a careful evaluation of children with lymphadenopathy by recording detailed history and appropriate physical examination to narrow down the diagnosis and avoid unnecessary invasive procedures.

Lymphadenopathy is typically classified into localized or generalized, with localized lymphadenopathy often associated with pathologies of the involved region [2]. Axillary lymphadenopathy can be due to benign and malignant conditions. The benign axillary lymphadenopathy is usually caused by skin infections, cat-scratch disease, and sarcoidosis [2]. Further, the malignant pathologies include lymphoma, leukemia, and skin cancers [2]. Here, we report the case of a child with axillary lymphadenopathy and night sweats. Biopsy findings revealed the diagnosis of Castleman disease, a rare etiology of lymphadenopathy in children.

Case Presentation

A 9-year-old boy was brought to the family medicine clinic with a right lump in the axilla. The child first noticed the swelling two months ago. The lump was not painful but its size has been increasing gradually. It was oval in shape with no overlying skin changes or discharge. No other lumps were noted. The swelling was associated with night sweats. However, there was no history of cough, fever, or weight loss. The child did not have any animal contact or insect bites. No history of upper respiratory tract symptoms or change in bowel habits was reported. The child did not complain of joint pain or stiffness and had no skin rash. He was evaluated previously by a number of general practitioners who informed the parents that the swelling was

likely related to an upper respiratory tract infection and offered antibiotic therapy for the child, which did not result in any improvement.

The patient had a history of recurrent acute tonsillitis. He underwent tonsillectomy four years ago with no complications. He was not taking any medications and was not known to have any allergies. His vaccination schedule was up-to-date. No history of recent travel or sick contact was reported. The child attained the developmental milestones at appropriate ages and he had a good performance in school. The family history was remarkable for hereditary blood disorders, including sickle cell disease and beta-thalassemia.

Upon examination, the patient had a smooth non-tender swelling in the right axilla. It was measuring around 4 x 4 cm. The overlying skin was normal with no erythema or ulceration. The swelling was not adherent to the overlying skin. It was mobile and had firm consistency. Head and neck examination revealed no pharyngeal congestion. No other lymph nodes were enlarged. Abdominal examination was normal with no evidence of splenomegaly or hepatomegaly. Other systems yielded normal examination findings.

Laboratory investigation showed mild anemia with a hemoglobin level of 11.5 g/dL, thrombocytosis with platelets count of 550,000/µL, and normal leukocytes count of 6500/µL. The inflammatory markers, including erythrocyte sedimentation rate (21 mm/h) and the C-reactive protein level (14 mg/dL), were elevated. Renal function tests showed normal blood urea nitrogen and creatinine levels. Hepatic function tests showed normal bilirubin, albumin, and transaminase levels. The viral serology panel, including HIV and hepatitis viruses, was negative.

The patient was referred to have an ultrasound examination of the right axilla. The examination demonstrated a well-circumscribed enlarged lymph node, measuring 3.4 cm in short axis, with the increased flow on color doppler. Subsequently, a core-needle biopsy was obtained from the lymph node for histopathological examination. It demonstrated proliferation of the follicular lymphoid tissues that were centered around penetrative vessels giving the appearance of “onion skin”. Such histopathological findings were in keeping with Castleman disease (Figure *1*).

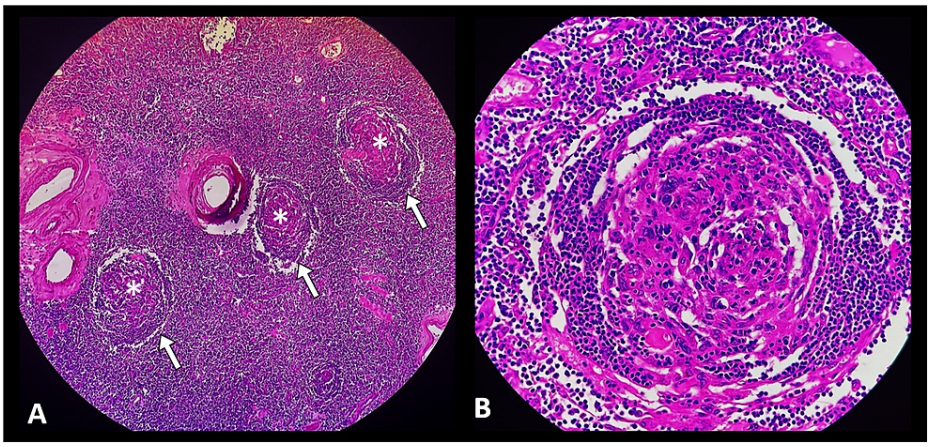

FIGURE 1: Histopathological images

(A) Histopathological image in low power-field demonstrates follicular lymphoid tissues centered (arrows) around penetrative vessels (asterisk) giving the appearance of “onion skin”

(B) High power-field image to demonstrate the appearance of “onion skin”

Subsequently, the patient underwent a contrast-enhanced thoracic computed tomography scan. The scan showed re-demonstrated the right axillary lymphadenopathy with no evidence of lymphadenopathy in other regions (Figure *2*). These findings represented the diagnosis of unicentric Castleman disease.

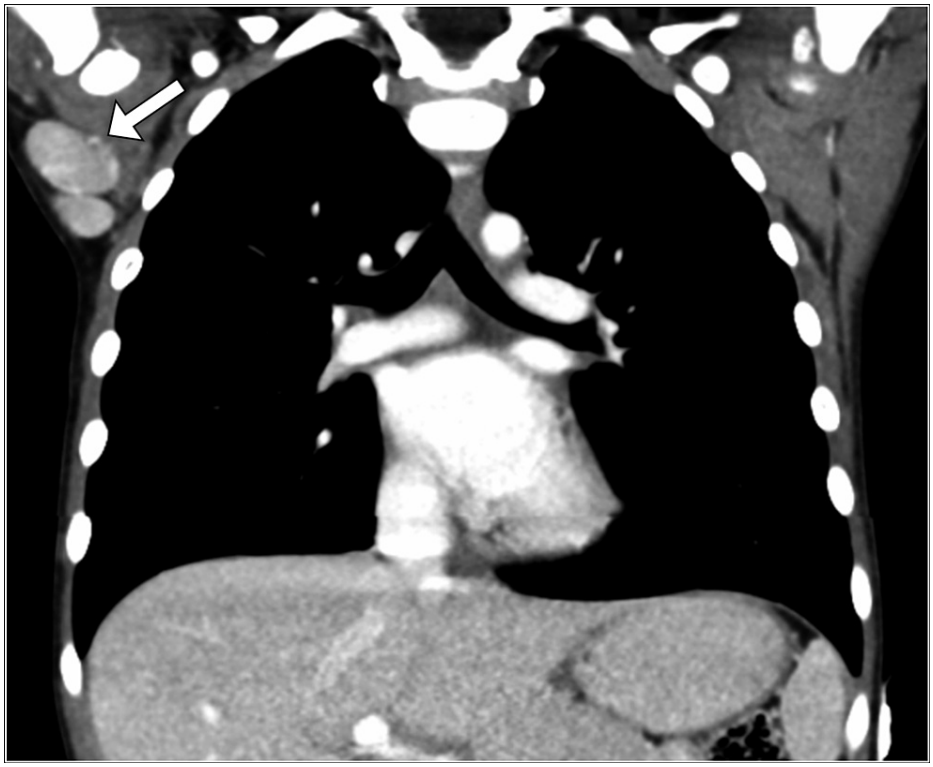

FIGURE 2: Contrast-enhanced CT chest

CT: computed tomography

The arrow shows right axillary lymphadenopathy, with no other enlarged lymph nodes

The patient underwent removal of the axillary mass lesion under general anesthesia. Following the operation, a significant improvement in the clinical condition was noted. The patient was followed for one year and had no signs to suggest recurrence.

Discussion

We reported the case of a unicentric Castleman disease in a child presenting with night sweats and axillary lymphadenopathy. Castleman disease, also known as angiofollicular lymph node hyperplasia, is a rare group of lymphoproliferative disorders with similar histopathological features [3]. Castleman disease has multiple hypotheses about its pathogenesis [3]. Some researchers suggested that it might be a neoplastic condition of a low-grade. This hypothesis is supported by a study finding that demonstrated monoclonality in a significant number of patients with unicentric Castleman disease [4]. It was also suggested that Castleman disease may arise because of an exaggerated response to a viral infection which could be the Epstein-Barr virus. While the virus has been identified in all patients with unicentric Castleman disease in one cohort [5], the study did not have a control group since the Epstein-Barr virus infection is very prevalent making the causal association not strong.

Castleman disease can be classified into unicentric and multicentric subtypes. In the unicentric subtype, the disease involves a single region of the body with enlarged lymph node groups. In contrast, the multicentric subtype involves multiple regions of lymphadenopathy [6]. In the present case, the computed tomography scan showed isolated axillary lymphadenopathy in keeping with the unicentric subtype. Jiang et al. performed a single-institution retrospective analysis of Castleman disease and found that only two out of 27 cases of unicentric Castleman disease involved the axillae, making it among the less commonly involved site for unicentric Castleman disease [7].

Castleman disease can develop at any age with the median age of diagnosis being 30 years [8]. However, it is more prevalent among younger individuals. Regarding the clinical manifestation, unicentric Castleman disease lacks the systemic constitutional symptoms in the vast majority of cases and it presents with a painless enlarged lymph node that is identified in physical examination or imaging studies [9]. If the lymph node is enlarged to a large size, it may present with a mass effect due to compression of the adjacent structures. In contrast, the multicentric type of Castleman disease involves systemic symptoms, including splenomegaly, hepatomegaly, night sweats, fever, weight loss, pleural effusion, peripheral edema, and ascites [9]. In the present case, the patient exhibited systemic symptoms despite that the disease was

localized into a single lymph node region, which is very rare [10].

Several laboratory markers can be deranged in patients with Castleman disease [3,11]. In the present case, the patient had elevated C-reactive protein and erythrocyte sedimentation rate, thrombocytosis, and anemia. Such abnormal laboratory findings were reported to be prevalent in both the unicentric and multicentric subtypes of Castleman disease [10]. In the present case, the abnormal laboratory parameters returned to the normal level as seen in the follow-up after 1 month from the resection of the axillary lymph node.

There are no imaging characteristic features for Castleman disease [9]. The diagnosis can be established by histopathological examination of the obtained biopsy specimen [9]. In the present case, we performed a contrast-enhanced computed tomography scan in order to rule out any other lymphadenopathies or pathologies since the patient exhibited systemic symptoms, which is atypical for patients with unicentric Castleman disease [6].

Complete surgical resection of the involved lymph nodes in patients with unicentric Castleman disease is the gold standard and results in complete resolution of the patient's complaints, as in the present case [6]. Unresectable unicentric Castleman disease may be rendered amenable to resection by medical therapy (e.g., rituximab, steroids), radiotherapy, or embolization [12]. Recurrence of unicentric Castleman disease is rare and is most likely related to incomplete surgical resection rather than a true recurrence [6,9]. Patients with Castleman disease may be at increased risk of Hodgkins's and non-Hodgkin's lymphoma and amyloidosis [6,8].

Conclusions

Castleman disease is a rare lymphoproliferative disorder with shared histopathological features. Unicentric Castleman disease usually presents with isolated asymptomatic lymphadenopathy. However, the present case demonstrated that patients with unicentric Castleman disease may exhibit systemic constitutional symptoms similar to that of the multicentric subtype. No imaging features are characteristic for Castleman disease and the diagnosis can be made by histopathological examination. Complete surgical resection of the involved lymph node is curative.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. University Institutional Review Board issued approval N/A. Case reports are waived by the institutional review board. Informed consent was taken from the parents. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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